

Remarks

The Examiner has required an election of species under 37 C.F.R. § 1.146, from within claims 2-6 and 11. Specifically, the Applicant is required to elect:

A) a single disclosed specie of cognitive disorder or a generic cognitive disorder not specifically claimed;

B) a single disclosed specie of clavulanic acid compound specifically claimed or clavulanic acid or an active ester form of clavulanic acid that is hydrolyzed in vivo to clavulanic acid, or a generic clavulanic acid compound not specifically claimed; and

C) a single disclosed specie of P-glycoprotein efflux pump inhibitor.

Applicant respectfully traverses the election of a specific disorder as required by the Examiner. Applicant believes that dementia, amnesia, and Alzheimer's Disease are known to people of ordinary skill in the art to be related by a common manifestation of cognitive symptoms. This relationship is reflected in the DSM-IV code of the American Psychiatric Association. In the DSM-IV, amnesia and dementia share the same code (294.8), and dementias and Alzheimer's Disease are classified under similar code prefixes (*i.e.* 290's). Neuroscience teaches that the cognitive symptoms akin to each disorder result from dysfunction of specific brain regions, particularly the cerebral cortex and hippocampus. As the Examiner noted, the primary etiology and pathophysiological course of each disorder may not be indistinct; nonetheless, each of those disorders are linked by a similar neuroanatomical locus of insult, namely the hippocampus and cerebral cortex. Notably, the hippocampus and cerebral cortex both utilize the amino acid glutamate as a major excitatory neurotransmitter, and it is this same neurotransmitter that the instant invention is directed to modulate.

The invention defined by claims 2-6 and 11 is drawn to a method of enhancing cognitive function by specifically modulating glutamate concentration in the brain. Although cognitively impaired patients may be diagnosed with a particular disorder, each of which may require a slightly different treatment regimen to achieve therapeutic efficacy as suggested by the Examiner, the claimed invention targets the shared symptoms of each of these disease states via the same mechanism of action, modulation of brain glutamate. In this respect, a search of treatments for cognitive deficits from dementia, amnesia, and Alzheimer's Disease is likely to be coextensive and Applicant does not believe that such a search is burdensome on the Examiner.

Finally, contrary to the assertion by the Examiner, the art in fact *does* recognize that dementia, amnesia, and Alzheimer's Disease are amenable to the same types of pharmacologic therapy. For example, drugs such as Piracetam, (an AMPA receptor potentiator) and Aricept (an acetylcholinesterase inhibitor), have both been used to treat

cognitive deficits associated with dementia, amnesia, and Alzheimer's Disease (see Jelic, V. et al., *Journal of Neurology, Neurosurgery & Psychiatry* 77(4):429-38 (2006)).

Accordingly, Applicant believes that the Examiner's requirement to elect a specific disease state from the aforementioned is improper, and requests reconsideration of the same leading to its withdrawal.

Should the Examiner nevertheless maintain the election requirement, pursuant to 37 CFR §1.143 Applicant elects as follows:

- A) disease: dementia
- B) compound: clavulanic acid
- C) P-glycoprotein efflux pump inhibitor: (2R)-anti-5-{3-[4-(10,11-difluoromethanodibenzosuber-5-yl)piperazin-1-yl]-2-hydroxypropoxy}quinoline.


The use of clavulanic acid to enhance cognitive performance and treat neurological disorders of cognition such as dementia is disclosed on page 15 of the instant application.

Applicant discloses the co-administration of NAALADase inhibitors with P-glycoprotein efflux inhibitors on page 13. The P-glycoprotein efflux pump inhibitor (2R)-anti-5-{3-[4-(10,11-difluoromethanodibenzosuber-5-yl)piperazin-1-yl]-2-hydroxypropoxy}quinoline is described in U.S. Patent Numbers 5,889,007; 5,874,434; 5,654,304 and 5,643,909, the specifications of which patents are expressly incorporated by reference. The elected P-glycoprotein efflux pump inhibitor is disclosed in U.S. 5,889,007 as compound Formula III in column 5 line 66 through column 6 line 36, and in the Examples. It is disclosed similarly in U.S. 5,874,434; 5,654,304 and 5,643,909. Pursuant to the foregoing election of species, claims 2-6 and 11 read on the elected species.

In addition, Applicant requests entry of the amendment to the specification transmitted herewith. The amendment corrects an inadvertent typographical error in the Application Serial No. of the parent application.

Applicant believes that the present application is now in condition for allowance and such action is respectfully requested. If there are any questions or comments that would speed prosecution of this application, the Examiner is invited to contact the undersigned by telephone at (317) 231-7776 or by e-mail at kevin.mclaren@btlaw.com.

Respectfully submitted,
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